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NTP Board of Scientific Counselors Meeting

**Oral Comments on the Proposed Revisions to the Listing Process for
the NTP Report on Carcinogens**

from
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on behalf of the Styrene Information and Research Center

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Good afternoon, I am Dr. Lorenz Rhomberg, a Principal at Gradient, an environmental consulting firm. My comments today are my own, but they were prepared under the sponsorship of the Styrene Information and Research Center.

Decisions on whether and how to list chemicals in the Report on Carcinogens are hazard identification decisions, and – even though they are not themselves regulations – they have profoundly important consequences for regulation and for use of the listed substances: It is, therefore, crucial that the decisions be made in a way that has high scientific credibility.

This demands a process that ensures: that all the relevant and useful scientific data be objectively examined; that questions about scientific interpretation and inference from these data be fully and transparently aired and debated; that these questions are forthrightly and critically evaluated by the decision-makers, and that the basis for their decisions is clear, adheres to principles of sound scientific reasoning, and refers to a set of clearly articulated, well defined, and scientifically suitable standards regarding the grounds for listing chemicals and placing them in listing categories.

In short, credible listing decisions need both a sound PROCESS – one that provides for an open debate on all relevant data, with input from stakeholders and the wider scientific community – but also sound REASONING for how judgments regarding cancer hazard are to be arrived at and the consequent listing decisions justified. Either one without the other is insufficient to ensure a scientifically credible listing process.

I (and many others) would argue that the current RoC listing procedure needs to reform BOTH its procedural structure AND its articulation of scientific standards for its judgments.

This said, the current proposals for revision of the listing process focus almost entirely on the procedure and say little about how the judgments are to be made and the listing categories defined.

I call in the Board of Scientific Counselors to raise this shortcoming in its review of the proposed changes, and I urge the Board to call for the inclusion of a significant undertaking – with input from the public – to better define the standards for listings and how scientific reasoning should be used to support those judgments.

This call is fully in accord with the so-called "roadmap" offered in the recent National Academy of Sciences review of the EPA formaldehyde assessment. That report called for more systematic and defined methodology for identifying relevant studies, for evaluating the outcomes, for critical evaluation of the basis for inferences from those outcomes, in a way that stresses attention to the degree of consistency (or lack thereof) among studies, integrates inferences across animal, human, and mechanistic data, considers mode of action, and articulates the reasoning behind scientific inferences that are drawn.

The NAS Roadmap cites several existing examples of evaluation processes with articulated methods for making scientific judgments, but it urges significant further thinking, integration, and development of standards and methods for conducting weight-of-evidence evaluations. This call from the NAS panel was not just for formaldehyde nor just for EPA, but addressed to the process of risk evaluation in the public sector generally.

I am glad to see that at least some of the NAS "Roadmap" recommendations are echoed in the recent changes to the NTP Proposed Process – chiefly those dealing with the identification of relevant studies, inclusion criteria, etc. (But these additions appeared only days ago in a revision – they did not appear in the version of the Proposed Process first released by the NTP for public comment.)

About how to consider weight of evidence for listing decisions, the NTP Proposed Process says only that it "provides an assessment of the level of evidence for human studies or experimental studies in applying the RoC listing criteria" and that it "integrates the overall body of evidence." It says little about HOW such judgments are to be made, and what standards of evidence should apply.

What is problematic about the current RoC listing standards?

- First, the definitions of listing categories is largely tautological and circular – a "known" human carcinogen is effectively defined as one for which the evidence is deemed sufficient to conclude that it is known – that is, the conclusion provides its own justification.
- The "reasonably anticipated" category is defined largely in terms of being "less than" this ill-defined standard.

- Moreover, the "reasonably anticipated" category has no defined lower limit – in a number of Board reviews of NTP RoC recommendations, we have often seen Counselors struggling with whether failing to list a chemical with only marginal evidence is somehow implying that there is no evidence at all. In short, the "reasonably anticipated" category needs a defined "top" and a defined "bottom."
- In practice, judgments seem to be driven more by "strength of evidence" (i.e., the existence of positive outcomes) than by "weight of evidence" (which considers consistency among studies and the scientific case for applicability of inferences, including mode of action).

The depth of understanding of processes of chemically induced carcinogenesis has increased markedly in recent years, and the current inferential processes used by NTP or recommended in the current revision do not reflect this knowledge. This will only get more pronounced as gene-expression data, high-throughput in vitro data, and other "21st Century" testing methods come into play. In short, a listing process that cannot articulate the basis for its inferences of hazard and cannot explain the scientific reasoning behind its classifications will lose credibility.

What is needed is for listing criteria to be defined in terms of the underlying scientific judgments and inferences that need to be made. We don't need absolute proof, but we do need standards for what constitutes sufficient basis for inferences and placement into listing categories – standards that stress presentation of reasoning and that follow an articulated weight-of-evidence methodology.

We ask that the Board of Scientific Counselors recognize

- that beside Procedure -- the CRITERIA FOR LISTING also need attention,
- that without this, the Board cannot fulfill its role of evaluating the soundness of listing decisions, and
- that this question is not yet sufficiently addressed in the NTP Proposed Process.
- The Board should ask that it has the full information needed – not only the data but also an evaluation of the inferential issues
- and also the time to engage in its key role as critical evaluator of the scientific soundness of listing proposals.
- This should include clearly articulated criteria against which to compare its scientific judgments that will determine appropriate listing decisions that have consistent meaning across chemicals. These criteria, once developed and applied, together with an open and transparent procedure for their consideration, will result in listing decisions that will win the support of the scientific community at large.